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Application No.10/511,527

OCT 10 2006 Amendment

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Previously Presented) Method for the detection and characterisation of primary tumours and separate areas of primary tumours, respectively, method comprising using sample material to isolate and concentrate cell clusters of tumour cells, followed by an analysis of the genetic changes in these isolated cell clusters.

2. (Previously Presented) Method according to claim 1, sample material consists of cell cultures, blood, urine, nipple aspiration fluid from the female breast or tissue from primary tumours.

3. (Previously Presented) Method according to claim 1, wherein polymorphic DNA of primary tumours or separate areas of primary tumours, and alterations therein, respectively, are recorded and compared with corresponding polymorphic DNA of cell clusters, and alterations therein, respectively.

4. (Previously Presented) Method according to claim 1, wherein DNA of the following polymorphic sequences are analysed: D7S522, D8S133, D8S258, D8S265, NEFL, D10S541, D10S1765, D10S579, D13S153, D16S400, D16S402, D16S413, D16S422, p53, BB1, BB2, CAII, CAIII, CAIV, CAV and/or D17S855.

5. (Previously Presented) Method according to claim 1, wherein the polymorphic DNA is reproduced before analysis.

6. (Currently Amended) Method according to claim 5, wherein the polymorphic DNA of three polymorphic sequences, D7S522, D8S256 D8S258, D16S400 or NEFL, D13S153, D17S855 or D10S541, D16S402, D16S422 are analysed together and/or reproduced.

7. (Previously Presented) Method according to claim 6, wherein the polymorphic DNA is reproduced prior to analysis by polymerase chain reaction (PCR).

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8. (Previously Presented) Method according to claim 7, wherein the polymorphic DNA is reproduced by using the following primer pairs:

GCAGGACATGAGATGACTGA and GTTATGCCACTCCCTCACAC (for D7S522);
GTTGAAGAATTGAGCCAACC and TTCTTCTGCACACITGGCAC (for BB1+2);
CTCGAGGTCTCATCCTCTTCC and GCAGAGGTGCACAAAGGAGTAA (for CAII);
AGGCCACAGAGGAAGATAACAG and CAGGTGTGGTAGATGCCAAAGA (for CAIII);
GCAACTTATCAAACCTGACC and AGAGTGGACTAGGAAATGCTAGGAG (for CAIV);
AGTCCTGACTGGAAATCGAT and TTGGCCAAATTACACACACCTTG (for CAV);
TTCCATTGTCICGGTT and AGTCTCCTCGTCTCACACCT (for D7S2550);
CAGTGCTGGAGTTGTTCAAG and CTGGGAGTCAAGTGTITTGG (for D7S2429);
TGCTAACGTCTGATTTGCC and AACGGTCATCTGTGTTCG (for D7S2467);
GGTGTGTTGTCATTACGCT and TTGCTGTAGAGGATGCAAT (for D7S478);
TTCGGGCTCTCTGTATAAAA and CCGAACGAGGATTTATITC (for D7S670);
AGCTGCCAGGAATCAACTGAGAG and GATGCTCACATAAAGGAGGGAGG (for D8S258);
CCAATACCTGCAGTAGTGCC and GAGCTGCTAACACATAAGGG (for NEFL);
CACCAACAGACATCTCACACC and CCAGTGAATAGTTCAGGGATGG (for D10S541);
AGGGTTATGTATAACCGACTCC and GTCTAACCCCTCGAGTTGTGG (for D13S153);
GGTCACAAATTGGACAGTAT and GAACCCCTCCATGCTGACATT (for D16S400);
GTACCCATGTACCCCCAATA and CAAAGCACCACATAGACTAA (for D16S402);
GAGAGGAAGGTGGAAATACA and GTTAGCAGAAATGAGAATAT (for D16S422);
AATAAATTCCCAC TGCCACTC and ATCCCCTGAGGGATACTATT (for p53);
GGATGGCCTTTAGAAAGTGG and ACACAGACTTGTCCACTGCC (for D17S855).

9. (Previously Presented) Method according to claim 5, wherein the reproduced DNA fragments are split and analysed by capillary electrophoresis.

10. (Previously Presented) Method according to claim 1, wherein the isolation or concentration of tumour cells cytokeratin-positive cells were isolated from sample material, and/or positive epithelial cells for tissue specific proteins.

11. (Previously Presented) Method according to claim 10, wherein epithelial cells are concentrated from sample material by means of density gradient centrifugation-if

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necessary after homogenisation in a solvent, and cytokeratin-positive and/or positive cell clusters from tissue specific proteins are then split off by means of immunomagnetic cell isolation.

12. (Previously Presented) Method according to claim 11, wherein the medium for the density gradient centrifugation is a hyper-osmotic medium.

13. (Previously Presented) Method according to claim 12, wherein the hyper-osmotic buffer consists of one of the following mediums: 13.8% (w/v) Diatrizoate and 8% (w/v) dextran 500 in H₂O (polymorphprep) or 13% (w/v) Nycodenz, 0.58% (w/v) NaCl and 5 mM Tricine-NaOH pH 7.4 in H₂O (Nycoprep).

14. (Previously Presented) Method according to claim 1, wherein genetic changes in the isolated cell clusters are analysed by means of cluster analysis.

15. (Previously Presented) Application of a method according to claim 1 for the molecular characterization of tumours or tumour sections or for the determination of clonality from cells clusters isolated from sample material as well as for the detection of a tumour to determine the tumour stage, the metastasising potential, therapy requirements, efficacy of therapy of a tumour or part thereof, as well as the assessment of the course of a disease or therapy.

16. (Previously Presented) Application according to claim 15 for the detection and/or characterisation of tumours or tumour areas of the following carcinomas: mamma-, ovarian-, colon-, gastric-, prostate and/or bladder carcinoma.